PTO/SB/08b(08-03)

Approved for use through 07/31/2008. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1986 Bases are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449B/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet of 1

	Complete if Known				
Application Number	10/622,068				
Filing Date	July 15, 2003				
First Named Inventor	Legarda Ibanez				
Art Unit	1614-1617				
Examiner Name	Unknown J. Kim				
Attorney Docket Number	55979/314570 (0200US)				

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials *	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T²
7	1	DERLET, R.W. et al., Anticonvulsivant Modification of Cocaine-Induced Toxicity in the Rat, Neuropharmacology, 1990, Vol. 29, No. 3, pp. 255-259.	
	2	DERLET, R.W. et al., Flumazenil Induces Seizures and Death in Mixed Cocaine-Diazepam Intoxications, Annals of Emergency Medicine, 1994, Vol. 23, No. 3, pp. 494-498.	
	3	MALBRAIN, M.L. et al., A Massive, Near-Fatal Cocaine Intoxication in a Body-Stuffer, Acta Clinica, Belgium, 1994, Vol. 49, No. 1, pp. 12-18.	
	4	UKI, F. et al., The Effect of Flumazenii Administration on Acute Cocaine Intoxication of Rats, Arukoru Kenkyu to Yakubutsu Izon, 1994, Vol. 29, No. 2, pp. 92-102.	
7	5	WOOLF, A., Cocsine Poisoning, Clinical Toxicology Review, May 1995, Vo. 18, No. 8.	
		·	

Signature Considered //14/04				1 / ' // *
------------------------------	--	--	--	------------

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Applicant's unique citation designation number (optional). Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Tredemark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450, DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

PTO/S8/08A (08-00)
Approved for use through 10/31/2002 OMB 0851-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
To persons are required to respond to a collection of information untess it contains a valid OMB control number Under the Paperwark Reduction Act of 199

Substitute for Form 1449/A/PTO

SEP 0 9 2005

(use as many sheets as necessary

Sheet	1	of	5	

Cor	nplete if Known
Application Number	10/622,068
Filing Date	July 15, 2003
First Named Inventor	Juan Legarda Ibanez
Group Art Unit	1614- 1619
Examiner Name	Not yet assigned J. Lim
Attorney Docket Number	55979-314570 (55979-0200)

	U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.'	U.S. Patent Number	Document Kind Code ² (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pagas, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
2	1.	6,455,276		Le Bourdelles et al.	09-24-2002	
12	2.	6,740,677		Xue et al.	05-25-2004	
	!					

	 	-				
		 				
	 	 				
v	 	<u> </u>				
	 	<u> </u>				
	 	 				
	 	 				
	ļ					
		ļ			_	,
		L				

	FOREIGN PATENT DOCUMENTS							
Examiner	I		Foreign Patent Oc		N	Date of Publication of	Pages, Columns, Lines, Where	
Initials	Cite No.1	Office ³	Number ⁴	Kind Code ^s (if known)	Name of Patentee or Applicant of Cited Document	Cited Document MM-DD-YYYY	Relevant Passages or Relevant Figures Appear	T ⁴
		╂╌┼╴						\vdash
								Ш
								Ш
								\square
			_					

	<u> </u>		
Examiner Signature		Date Considered	4/14/06

¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language translation is attached.

PTO/S8/08B (08-00)

Approved for use through 10/31/2002 OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

	Cor	nplete if Known
Substitute for Form 1449/A/PTO	Application Number	10/622,068
INFORMATION DISCLOSURE	Filing Date	July 15, 2003
INFORMATION DISCLOSURE	First Named Inventor	Juan Legarda Ibanez
STATEMENT BY APPLICANT	Group Art Unit	1614-1617
(use as many sheets as necessary	Examiner Name	Not yet assigned J. Kim
Sheet 2 of 5	Attorney Docket Number	55979-314570 (55979-0200)

		OTHER INFORMATION - NON PATENT LITERATURE DOCUMENTS	
Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city end/or country where published	T ²
	3.	Baldwin, H.A., et al., "Flumazenil Prevents the Development of Chlordiazepoxide	
7-		Withdrawal in Rats Tested in the Social Interaction Test of Anxiety,"	
	l	Psychopharmacology, Vol. 97, No. 3, pp. 424-426 (1989) (Abstract Only)	
	4.	Brooks-Kayal-A.R., et al., "Human Neuronal γ-Aminobutyric Acid _A Receptors:	
1		Coordinated Subunit mRNA Expression and Functional Correlates in Individual Dentate	
		Granule Cells," J. Neuroscience, Vol. 19, No. 19, pp. 8312-8318 (1999)	
	5.	Criswell, H.E., et al., "Effect of Zolpidem on Gamma-aminobutyric Acid (GABA)-	
		Induced Inhibition Predicts the Interaction of Ethanol with GABA on Individual Neurons	
		in Several Rat Brain Regions," J. Pharmacol. Exp. Therp., Vol. 273, No. 1, pp. 526-536	
		(1995) (Abstract Only)	
	6.	Ferrara, G., et al., "Increased Expression of the Neuropeptide Y receptor Y1 Gene in the	
,		Medical Amygdala of Transgenic Mice Induced by Long-term Treatment with	
		Progesterone or Allopregnanolone," J. Neurochemistry, Vol. 79, pp. 417-425 (2001)	
	7.	Frostholm, A., et al., "Harmaline-induced Changes in Gamma Aminobutyric Acid,	
1		Receptor Subunit mRNA Expression in Murine Olivocerebellar Nuclei," Molecular	
	<u> </u>	Brain Research, Vol. 85, pp. 200-208 (2000)	
	8.	Gee, K., et al., "A Putative Receptor for Neurosteroids on the GABAA Receptor	
		Complex: The Pharmacological Properties and Therapeutic Potential of Epalons," Crit.	
		Rev. Neurobiol, Vol. 9, Nos. 2-3, pp. 207-227 (1995)	
	9.	Gulinello, M., et al., "Progesterone Withdrawal Increases the a4 Subunit of the GABAA	
		Receptor in Male Rats in Association With Anxiety and Altered Pharmacology – A	
		Comparison With Female Rats," Neuropharmacology, Vol. 43, pp. 701-714 (2000)	
ļ	10.	Gulinello, M., et al., "Anxiogenic Effects of Neurosteroid Exposure: Sex Differences and	
		Altered GABA _A Receptor Pharmacology in Adult Rats," J. Pharmacology and	
		Experimental Therapeutics, Vol. 305, No. 2, pp. 541-548 (2003)	
	11.	Hawkinson, J.E., "Substituted 3β-Phenylethynyl Derivatives of 3α-Hydroxy-5α-pregnan-	
1		20-one: Remarkably Potent Neuroactive Steroid Modulators of γ-Aminobutyric Acid _A	
		Receptors," J. Pharmacology and Experimental Therapeutics, Vol. 287, No. 1, p. 198-	
		207 (1998)	
1	12.	Hogenkamp, D.J., et al., "Synthesis and in Vitro Activity of 3β-Substituted-3α-	
\ ,		Hydroxypregnan-20-ones: Allosteric Modulators of the GABA _A Receptor," J. Med.	
-V_		Chem., Vol. 40, pp. 61-72 (1996)	L
:	13.	Hsu, F et al., "Progesterone Withdrawal Reduces Paired-Pulse Inhibition in Rate	
7	Γ	Hippocuampus: Dependence on GABA _A Receptor α4 Subunit Upregulation," J.	
	L	Neurophysiol., Vol. 89, pp. 186-198 (2003)	<u> </u>

Examiner Signature	Date Considered	4/14/06	
Signature	Considered	1111/06	

PTO/SB/088 (08-00)
Approved for use through 10/31/2002 OMB 0851-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for Form 1449/A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary

Sheet 3 of | 5

Cor	nplete if Known
Application Number	10/622,068
Filing Date	July 15, 2003
First Named Inventor	Juan Legarda Ibanez
Group Art Unit	1614-1617
Examiner Name	Not yet assigned J. Kim
Attorney Docket Number	55979-314570 (55979-0200)

		OTHER INFORMATION - NON PATENT LITERATURE DOCUMENTS	
Examin Initiats	No	include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the	T²
	14.	Krogsgaard-Larsen, P., et al., "GABAA Agonists and Partial Agonists: THIP	
7	$ \bot $	(Gaboxadol) as a Non-Opioid Analgesic and a Novel Type of Hypnotic," Biochemical	
		Pharmacology, Vol. 68, pp. 1573-1580 (2004)	
, 15.		Holt, R.A., et al., "Chronic Treatment with Diazepam or Abecarnil Differently Affects	·
		the Expression of GABA _A Receptor Subunit mRNAs in the Rat Cortex,"	
		Neuropharmacology, Vol. 35, Nos. 9 & 10, pp. 1457-1463 (1996); Abstract only.	
	16.	Lan, N.C., et al., "Differential Responses of Expressed Recombinant Human Gamma-	
		aminobutyric acid, Receptors to Neurosteroids," J. Neurochem., Vol. 57, No. 5, pp.	
		1818-1821 (1991) (Abstract Only)	
	17.	Lee, C., et al., "Effects of Benzodiazepine Receptor Antagonist, Flumazenil, on	
1,1		Antinociceptive and Behavioural Responses to the Elevated Plusmaze in Mice,"	
`		Neuropharmacology, Vol. 30, No. 12A, pp. 1263-1267 (1991) (Abstract Only)	
	18.	Medina, J.H., et al., "Overview-Flavonoids: A New Family of Benzodiazepine Receptor	
		Ligands," Neurochemical Research, Vol. 22, No. 4, pp. 419-425 (1997)	
		Smith, S.S., et al., "Neurosteroid Administration and Withdrawal Alter GABA _A Receptor	
		Kinetics in CA1 Hippocamppus of Female Rats," J. Physiol., Vol. 567, Pt. 2. pp. 421-	
		436 (2005) (Abstract Only)	
	20.	Sur, C., et al., "Preferential Coassembly of α4 and δ Subunits of the γ-Aminobutyric	
		Acid Receptor in Rat Thalamus," American Society of Pharmacology and Experimental	
		Therapeutics, Vol. 56, pp. 110-115 (1998)	
21.			
		Emphasis on Benzodiazepine-induced Hyperphagia and Its Antagonism by Flumazenil	
and RO 15-3505," J. Vet. Pharmacol. Ther., Vol. 12, No. 2, pp. 147-156 (1989),		and RO 15-3505," J. Vet. Pharmacol. Ther., Vol. 12, No. 2, pp. 147-156 (1989); Abstract of	nly
	22.	Whittemore, E.R., et al., "Pharmacology of the Human Gamma-aminobutyric acid,	7
		Receptor Alpha 4 Subunit Expressed in Xenopus Laevis Oocytes," Mol. Pharmacol.,	
y	'	Vol. 50, No. 5, pp. 1364-1375 (1996) (Abstract Only)	
	23.	Wisden, W., et al., "Cloning, Pharmacological Characteristics and Expression Pattern of	
7	'	the Rat GABA _A Receptor Alpha 4 Subunit," FEBS Lett., Vol. 289, No. 2, pp. 227-230	
		(1991) (Abstract Only)	

Considered	Examiner Signature		Date Considered	4/14/06
------------	-----------------------	--	--------------------	---------

¹Unique citation designation number. ²Applicant is to place a check mark here if English language translation is attached.

PTC/SB/088 (08-00)

Approved for use through 10/31/2002 OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for Form 1449/A/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Complete if Known		
			•	Application Number	10/622,068	
			I DICCI OCUDE	Filing Date	July 15, 2003	
				First Named Inventor	Juan Legarda Ibanez	
			BY APPLICANT	Group Art Unit	1614-1617	
(use as many sheets as necessary		Examiner Name	Not yet assigned J. Kim			
Sheet	4	of	5	Attorney Docket Number	55979-314570 (55979-0200)	

		OTHER INFORMATION - NON PATENT LITERATURE DOCUMENTS	
Examiner Initials	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), data, page(s), volume-issue number(s), publisher, city and/or country where published	T²
	24.	Adkins, C.E., et al., "α4β3δ GABA _A Receptors Characterized by Fluorescence	
1-	1	Resonance Energy Transfer-derived Measurements of Membrane Potential," J.	
		Biological Chemistry, Vol. 276, No. 42, pp. 38934-38939 (2001)	
1	25.	Akk, G., et al., "Activation of GABA(A) Receptors Containing the alpha4 subunit by	
		GABA and Pentobarbital," J. Physiol., Vol. 556, Part 2, , pp. 387-399 (2004)	
$\neg T$	26.	Banerjee, P.K., et al., "Alterations in GABAA Receptor al and a4 Subunit mRNA Levels	
- 1		in Thalamic Relay Nuclei Following Absence-like Seizures in Rats," Experimental	
		Neurology, Vol. 154, pp. 213-223 (1998)	
	27.	Biggio, G., et al., "GABAA-receptor Plasticity During Long-Term Exposure to and	
		Withdrawal from Progesterone," Int. Rev. Neurobiol., Vol. 46, pp. 207-241 (2001), Abstract	on
	28.	Burt, D.R., "Alpha Subunit Position and GABA Receptor Function," Science's STKE,	′
-1		No. 270, PE5, pp. 1-2 (2005)	
+	29.	Lovick, T.A., et al., "Changes in GABA, Receptor Subunit Expression in the Midbrain	
.]		During the Oestrous Cycle in Wistar Rats," Neuroscience, Vol. 131, pp. 397-405 (2005)	
1	30.	Lujan, R., et al., "Glutamate and GABA Receptor Signalling in the Developing Brain,"	
- 1		Neuroscience, Vol. 130, pp. 567-580 (2005)	
	31.	Mody, I., "Distinguishing between GABA _A Receptors Responsible for Tonic and Phasic	
		Conductances," Neurochemical Research, Vol. 26, Nos. 8-9, pp. 907-913 (2001)	
	32.	Porter, B.E., et al., "Heterogeneous GABA(A) Receptor Subunit Expression in Pediatric	
1		Epilepsy Patients," Neurobiol. Dis., Vol. 18, No. 3, pp. 484-491 (2005) (Abstract Only)	
	33.	Quirk, G.J., et al., "Inhibition of the Amygdala: Key to Pathological States?," Ann. N.Y. Acad. Sci., Vol. 985, pp. 263-272 (2003)	
	34.	Rissman, R.A., et al., "Subregional Analysis of GABAA Receptor Subunit mRNAs in the	
1		Hippocampus of Older Persons with and without Cognitive Impairment," J. Chemical	
		Neuroanatomy, Vol. 28, pp. 17-25 (2004)	
	35.	Saitoh, K., et al., "Nigral GABAergic Inhibition Upon Mesencephalic Dopaminergic	
1/		Cell Groups in Rats," Eur. J. Neurosci., Vol. 19, No. 9, pp. 2399-2409 (2004) (Abstract	
Ψ		Only)	
	36.	Sedvall, G., et al., "Recent Advances in Psychiatric Brain Imaging," Acta Radiol. Suppl.,	
2	1	Vol. 374, pp. 113-115 (1990) (Abstract Only)	
<i>[</i>	<u> </u>		
			

	·	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	·
Examiner Signature		Date Considered	4/14/06
			A

PTC/SB/08B (08-00)

Approved for use through 10/31/2002 OMB 0851-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

	Complete if Known		
Substitute for Form 1449/A/PTO	Application Number	10/622,068	
INFORMATION DICCLOSURE	Filing Date	July 15, 2003	
INFORMATION DISCLOSURE	First Named Inventor	Juan Legarda Ibanez	
STATEMENT BY APPLICANT	Group Art Unit	1614- (617)	
(use as many sheets as necessary	Examiner Name	Not yet assigned. J. Kim	
Sheet 5 of 5	Attorney Docket Number	55979-314570 (55979-0200)	

		OTHER INFORMATION - NON PATENT LITERATURE DOCUMENTS	
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the Item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-Issue number(s), publisher, city and/or country where published	T²
	37.	Smith, A.J., et al., "Effect of a Subunit on Allosteric Modulation of Ion Channel	
		Function in Stably Expressed Human Recombinant y-Aminobutyric Acid, Receptors	
7		Determined Using ³⁶ Cl Ion Flux," <i>Molecular Pharmacology</i> , Vol. 59, No. 5, pp. 1108-1118 (2001)	
38. Smith,		Smith, S.S., et al., "GABA _A Receptor α4 Subunit Suppression Prevents Withdrawal Properties of an Endogenous Steroid," Nature, Vol. 392, pp. 926-930 (1998)	
	39.	Weinbroum, A.A., et al., "Flumazenil Potentiation of Postoperative Morphine Analgesia," Clin J. Pain, Vol. 16, No. 3, pp. 193-199 (2000) (Abstract Only)	
	40.	White, J.A., et al., "Antagonism of a Nicotine Plus Midazolam Discriminative Cue in Rats," Behav. Pharmacol., Vol. 5, No. 3, pp. 361-355 (1994) (Abstract Only)	
•	41.	Yang, W., "Cloning and Characterization of the Human GABA _A Receptor Alpha 4 Subunit: Identification of a Unique Diazepam-Insensitive Binding Site," Eur. J. Pharmacol., Vol. 291, No. 3, pp. 319-325 (1995) (Abstract Only)	
	42.	Zheng, T.M., et al., "Chronic Flumazenil Alters GABA _A Receptor Subunit mRNA Expression, Translation Product Assembly and Channel Function in Neuronal Cultures," J. Pharmacol. Exp. Ther., Vol. 277, No. 1, pp. 525-533 (1996) (Abstract Only)	
2	43.	Zheng, T.M., et al., "Changes in γ-aminobutyrate Type A Receptor Subunit mRNAs, Translation Product Expression, and Receptor Function During Neuronal Maturation in vitro," Proc. Natl. Acad. Sci. USA, Vol. 91, pp. 10952-10956 (1994)	·
/			
	<u> </u>		<u> </u>

Examiner Signature	Date Considered	4/14/06